Breast cancer screening and prevention: Update from the USPSTF

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What we’re going to do today

• Overview of the USPSTF and how it does its work
• Current recommendations regarding breast and ovarian cancer
• Future challenges related to screening and prevention

• Disclosure: Member, USPSTF
Screening can also be controversial! Especially when recommendations are updated.
The Breast Brouhaha

By GAIL COLLINS
Published: November 18, 2009

Everyone has been trying to come up with a good nickname for the 10 years we're concluding next month. Terror Era really sounds like too much of a downer. How about the Decade of Medical Backtracking?

Somewhere between the reports that Pap smears and tests for prostate cancer aren't all they were cracked up to be and the news that a high fiber diet doesn't do anything to prevent cancer, the health establishment began looking decidedly nonomniscient. Then this week, a federal task force reported that most women don't need annual mammograms.

Even more fascinating, they suggested that doctors stop
“If the world of primary care physicians had a supreme wizarding council that only weighed in on screening tests and pills promising to head off disease, it would be called the US Preventive Services Task Force.”
Who is this USPSTF? And can we stop them?!?!?

Established in 1984, makes recommendations on clinical preventive services to primary care clinicians such as:

- screening tests
- counseling services
- preventive medications

- Services are offered in a primary care setting or referable from primary care
- Recommendations apply to adults and children with no signs or symptoms
- Do not consider financial impact
Who is on the USPSTF?

• Independent panel of 16 non-Federal, voluntary experts in:

• Carefully vetted for financial conflict of interest

• Serve 4 year terms as unpaid volunteers (3 meetings per year + many phone calls + much reading and study). About 10% FTE.

• Specialties represented:
  – Family medicine, internal medicine, pediatrics, obstetrics/gynecology, nursing, behavioral health
Do USPSTF recommendations matter?

From the Affordable Care Act:
“A group health plan and a health insurance issuer offering group or individual health insurance coverage shall provide coverage for and shall not impose any cost sharing requirements for evidence-based items or services that have a rating of A or B in the current recommendations of the USPSTF”
Steps the USPSTF Takes to Solicit Public Input and Make a Recommendation: Step 1

Create Research Plan

- **Draft Research Plan**
  Task Force members work with researchers from an Evidence-based Practice Center (EPC) to create a draft Research Plan that guides the recommendation process.

- **Invite Public Comments**
  The draft Research Plan is posted on the USPSTF Web site for public comment.

- **Finalize Research Plan**
  The Task Force and EPC review all comments, address them as appropriate, and create a final Research Plan.

Compile Evidence Report

Develop Recommendation

Disseminate Recommendation
Example of an analytic framework: Colorectal cancer screening
Steps the USPSTF Takes to Solicit Public Input and Make a Recommendation: Step 2

Create Research Plan

Compile Evidence Report

Draft Evidence Report
Using the final Research Plan, the research team at the EPC independently gathers and reviews the available published evidence and creates a draft Evidence Report. The draft Evidence Report is critiqued by external national subject matter experts.

Invite Public Comments
(Beginning in 2013)
The draft Evidence Report is posted on the USPSTF Web site for public comment.

Finalize Evidence Report
The EPC reviews all comments, addresses them as appropriate, and revises the Evidence Report.

Develop Recommendation

Disseminate Recommendation
Steps the USPSTF Takes to Solicit Public Input and Make a Recommendation: Step 3

Create Research Plan

Compile Evidence Report

Develop Recommendation

Draft Recommendation
Task Force members discuss the Evidence Report and deliberate on the effectiveness of the service. Based on the discussion, Task Force members create a draft Recommendation.

Invite Public Comments
The draft Recommendation is posted on the USPSTF Web site for public comment. (The Evidence Report is updated and published.)

Finalize Recommendation
The Task Force reviews all comments, addresses them as appropriate, and creates a final Recommendation. Members vote to ratify the final Recommendation.

Disseminate Recommendation
Steps the USPSTF Takes to Solicit Public Input and Make a Recommendation: Step 4

Create Research Plan

Compile Evidence Report

Develop Recommendation

Disseminate Recommendation

Publish and Disseminate Final Recommendation

The final Recommendation and supporting materials are posted on the USPSTF Web site at www.uspreventiveservicestaskforce.org. Final Recommendations also are made available through electronic tools, peer-reviewed journals, and consumer guides.
Our overarching questions:
1. What is the net benefit?
2. How certain is the evidence?

Net Benefit = Benefits – Harms

There are always harms, and when you start with perfectly healthy, asymptomatic people it is especially important that they be minimal!
### USPSTF Grades of Recommendation

<table>
<thead>
<tr>
<th>Certainty of Net Benefit</th>
<th>Magnitude of Net Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Substantial</td>
</tr>
<tr>
<td>High</td>
<td>A</td>
</tr>
<tr>
<td>Moderate</td>
<td>B</td>
</tr>
<tr>
<td>Low</td>
<td></td>
</tr>
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</table>
Keys to USPSTF Success: Why people (sometimes) pay attention to our recommendations

• The USPSTF is an independent entity, with volunteers experts
• Free of conflict of interest: professional, financial, and commercial
• Process is transparent and clear
• Process is rigorously evidence-based
• Stakeholders engaged throughout with opportunities for public/private partnership
Current recommendations from USPSTF related to breast and ovarian cancer
Breast cancer screening

- **Good old days**: just get a mammogram every year starting at 40 (baseline at 35!)
- **Now we know**:
  - Overdiagnosis is an important concern
  - We have discovered BRCA
  - For carefully selected women, chemoprevention with raloxifene or tamoxifen provides net benefit
Breast cancer screening: current USPSTF recommendations (2009)

• Biennial mammography in women age 50 to 74 years (B)
• Decision to start before age 50 should be individualized (C), due to small net benefit for average risk women
• Insufficient evidence regarding women 75 years and older, newer technologies, and CBE (I)
• Recommend against primary care physicians teaching self breast examination (D)
Recent report: 25 year follow-up of Canadian RCT in women 40-59

89,835 women received breast exam by clinician, then study coordinator randomized to mammography or usual care. Any positive mammogram or abnormal exam referred to study surgeon.
Recent report: 25 year follow-up of Canadian RCT in women 40-59

- From 1988 to 1996, coordinating centre determined cause of death. From 1996 to 2005, record linkage was used to determine outcomes.
- No difference in all-cause (left) or breast-cancer specific mortality (right).
- With improved awareness of breast cancer, perhaps women were bringing lumps to their physician’s attention sooner? Also better treatment, widespread use of tamoxifen improved outcomes.

![Graphs showing survival probability over years after enrolment for control and mammography arms.](image-url)
Criticisms and responses

- Women with positive physical exam were preferentially assigned to mammography group
  - Percentage of abnormal exams similar between groups
  - Even if you exclude prevalent breast cancers detected during initial round, still no benefit.
- Women in screening group were at higher baseline risk
  - After screening period ended in 1988, no difference between groups in breast cancer incidence (5.8% vs 5.9%)
- Women in the control group received mammograms outside the study
  - Routine mammography not covered or widely used till after study period. Most mammograms were diagnostic, and adjusted analysis still found no benefit
What is coming?

- USPSTF has begun process of revising mammography recommendations for **late 2014**
- Issues that may be addressed:
  - Can we identify high risk women in their 40’s who should definitely be screened?
  - Can we provide any guidance regarding women over 75?
  - What is impact of digital mammography?
  - Different start/stop ages, intervals?
Breast cancer chemoprevention: current USPSTF recommendations (2013)

• The USPSTF recommends that clinicians engage in shared, informed decision-making with women who are at increased risk for breast cancer about medications to reduce their risk. For women who are at increased risk for breast cancer and at low risk for adverse medication effects, clinicians should offer to prescribe risk-reducing medications, such as tamoxifen or raloxifene (B).

• The USPSTF recommends against the routine use of medications, such as tamoxifen or raloxifene, for risk reduction of primary breast cancer in women who are not at increased risk for breast cancer (D).
Clinician tasks related to breast cancer screening and prevention


1. If elevated (> 1.6% 5 year risk) refer to table that reports benefits and harms by:
   – breast cancer risk
   – age
   – race
   – drug used to prevent breast cancer
3. Refer to net benefit tables (by race and uterine status)

<table>
<thead>
<tr>
<th>5-year projected risk of IBC (%)</th>
<th>Tamoxifen vs. Placebo (with uterus)</th>
<th>Raloxifene vs. Placebo (with uterus)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>60-69</td>
<td>70-79</td>
</tr>
<tr>
<td>1.5</td>
<td>-133</td>
<td>-310</td>
</tr>
<tr>
<td>2.0</td>
<td>-105</td>
<td>-283</td>
</tr>
<tr>
<td>2.5</td>
<td>-78</td>
<td>-255</td>
</tr>
<tr>
<td>3.0</td>
<td>-51</td>
<td>-228</td>
</tr>
<tr>
<td>3.5</td>
<td>-25</td>
<td>-202</td>
</tr>
<tr>
<td>4.0</td>
<td>3</td>
<td>-175</td>
</tr>
<tr>
<td>4.5</td>
<td>29</td>
<td>-148</td>
</tr>
<tr>
<td>5.0</td>
<td>56</td>
<td>-121</td>
</tr>
<tr>
<td>5.5</td>
<td>83</td>
<td>-95</td>
</tr>
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<td>6.0</td>
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<td>6.5</td>
<td>135</td>
<td>-42</td>
</tr>
<tr>
<td>7.0</td>
<td>162</td>
<td>-15</td>
</tr>
</tbody>
</table>

- Using BCPT data and WHI baseline rates
- Combining RR from BCPT and STAR using WHI baseline rates

- □ Strong evidence of benefits outweighing risks
- □ Moderate evidence of benefits outweighing risks
- □ Benefits do not outweigh risks

5-year projected risk of IBC is ≥1.67%
Screening for BRCA mutation: current USPSTF recommendation

- The USPSTF recommends that primary care providers screen women who have family members with breast, ovarian, tubal, or peritoneal cancer with one of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (BRCA1 or BRCA2). Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing (B).

- The USPSTF recommends against routine genetic counseling or BRCA testing for women whose family history is not associated with an increased risk for potentially harmful mutations in the BRCA1 or BRCA2 genes (D).
Screening for BRCA mutation

1. Determine if any family history of breast cancer using one of four tools (simplest below)

2. [http://www.uspreventiveservicestaskforce.org/uspstf12/brcatest/brcatestfinalrstab.htm#tab1](http://www.uspreventiveservicestaskforce.org/uspstf12/brcatest/brcatestfinalrstab.htm#tab1)

**Table 4. Pedigree Assessment Tool***

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer at age ≥50 y</td>
<td>3</td>
</tr>
<tr>
<td>Breast cancer at age &lt;50 y</td>
<td>4</td>
</tr>
<tr>
<td>Ovarian cancer at any age</td>
<td>5</td>
</tr>
<tr>
<td>Male breast cancer at any age</td>
<td>8</td>
</tr>
<tr>
<td>Ashkenazi Jewish heritage</td>
<td>4</td>
</tr>
</tbody>
</table>

*From reference 17. A score of ≥8 is the optimum referral threshold.† For every family member with a breast or ovarian cancer diagnosis, including second- or third-degree relatives.
Screening for BRCA mutation

3. If positive on one of these breast cancer risk tools
   – Order genetic counseling, they will decide whether to order BRCA test
   – Order test yourself and interpret

NYT July 13, 2012: “While it might not always be immediately obvious to patients, some counselors offering them advice in hospitals and doctors’ offices work for the commercial genetic testing companies, not for the hospitals or doctors themselves.”
Ovarian cancer screening: current USPSTF recommendations

- The USPSTF recommends against screening for ovarian cancer in women (D).

- PLCO: 78,000 average risk women randomized to ultrasound (4 yrs) + CA-125 (6 yrs) annually. After up to 13 years follow-up, no difference in ovarian cancer mortality

- What do other say?
  - ACOG: does not recommend screening in asymptomatic women
  - ACS: may offer pelvic exam + ultrasound + CA-125 to high risk women
UK Collaborative Trial of Ovarian Cancer Screening Protocol (results due 2014)

- 200,000 randomized to no screening, annual ultrasound, or annual CA-125
- CA-125 used patient-specific definition of abnormal
- If computer algorithm at central site detects pattern of increase (regardless of level) patient referred to highly trained, monitored center for either:
  - Moderate risk increase: ultrasound
    - If negative repeat CA-125 and USN in 3 mos
  - High risk increase: surgery
- Preliminary results encouraging – only 1% required surgery, 5 of 16 had ovarian cancer. But final mortality data not yet known
But can UKCTOCS strategy work in decentralized US health “system”? 

- Where things can go wrong with ovarian CA screening:
  - Patient never sees physician
  - Physician does not order test
  - Local lab does not report accurate CA-125
  - Algorithm is not interpreted correctly or is not available or is not used
  - Algorithm recommendation is ignored
  - Ultrasound is of poor quality or tech is poorly trained
  - Recall for follow-up is at wrong interval
Screening challenges:

Overdiagnosis and the increasing Complexity of Recommendations
Percent of men with prostate cancer on autopsy (1996 Detroit trauma victims)

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>African-American</th>
<th>Caucasian</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>30-39</td>
<td>31%</td>
<td>31%</td>
</tr>
<tr>
<td>40-49</td>
<td>43%</td>
<td>37%</td>
</tr>
<tr>
<td>50-59</td>
<td>46%</td>
<td>44%</td>
</tr>
<tr>
<td>60-69</td>
<td>70%</td>
<td>65%</td>
</tr>
<tr>
<td>70-79</td>
<td>81%</td>
<td>83%</td>
</tr>
</tbody>
</table>
Overdiagnosis of cancer

• **Old thinking**: no cancer $\rightarrow$ precancerous lesion $\rightarrow$ asymptomatic cancer $\rightarrow$ symptomatic cancer $\rightarrow$ death

• **New thinking**: several possible paths
  – Cancer progresses, cause symptoms, then death
  – Progresses and causes clinical symptoms, but not death, and is treatable
  – Grows slowly but never causes any symptoms
  – Precancerous lesions that regress
Incidence and mortality: Screening effective

- We begin a cancer screening program in 1990.
- We detect more cancer than before.
- After a few years, death rates due to that cancer begin to decline.
Top graph: widespread mammography for women in 40’s began in mid 1980’s

Middle graph: Large jump in incidence of early stage cancer: from 112 to 234 cases/100,000/year (blue line)

So far so good, right?

But by now, we should have seen similar decline in late stage cancer.

But, we have not: late stage only decreased from 102 to 94 cases/100,000/year (red line)
Breast cancer screening and prevention overview for the clinician

1. Assess personal risk using Breast Cancer Risk Assessment Tool (Gail model)
2. Assess family history using Pedigree Assessment Tool
3. Possibly refer for genetic counseling
4. Review net benefit tables to determine whether candidate for chemoprevention
5. Discuss all of this with the patient

That’s a lot to do!!! What can we do to help clinicians and patients?
A way forward

Overdiagnosis
- Better risk stratification, to avoid overscreening low risk persons
- Better biomarkers
- Increasing comfort with watchful waiting strategies

Increasing complexity
- Centralized delivery of screening and prevention
  - Better quality control
  - Guaranteed contact with entire population
  - Less over and under screening
- Decision-making tools for patients
- Further advances in genomics – better refinement of risk
Thank you!